Abstract of the Invention

This invention relates to the AIB1 protein as a coactivator that potentiates the transcriptional activity of nuclear hormone receptors. The gene is amplified in a subset of human breast cancers. One splice variant of AIB1 transcribes a mRNA that lacks the exon 3 sequence. Δ3-AIB1 mRNA encodes a 130 kDa protein that lacks the N-terminal basic helix-loop-helix and a portion of the PAS dimerization domain. This 130 kDa protein was detected in MCF-7 breast cancer cells at levels 5-10% of the full length protein, whereas in non transformed mammary epithelium lines the Δ3-AIB1 protein is present at significantly lower levels compared to the full length AIB1. The abundance of Δ3-AIB1 mRNA is increased in human breast cancer specimens relative to that in normal breast tissue. Functional reporter gene assays revealed that the ability of Δ3-AIB1 to promote transcription mediated by the estrogen or progesterone receptors was significantly greater than that of the full-length protein. The Δ3-AIB1 isoform was also more effective than AIB1 in promoting transcription induced by epidermal growth factor. Thus, over expression of Δ3-AIB1 plays an important role in sensitizing breast tumor cells to hormone or growth factor stimulation.